Tavola Rotonda: «Il Trapianto renale»

9 maggio 2023

Moderatori: Cristiana Dente, Piera Rossetto Casel

Quando il trapianto perde la sua efficacia, il percorso di rientro in dialisi

Gabriele Donati
SC Nefrologia Dialisi e Trapianto renale

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
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No Consensus on the Definition of a Failing Kidney Allograft

- **Stable but low allograft function (GFR < 20 ml/min)**
- **Declining function**
- **Return to renal replacement therapy**

Lubetzky M et al. Am J Transplant 2021; 21: 2937-2949

Outcomes after a First-time Kidney Transplantation

vol 2 Table 7.3 Trends in 1-, 5-, & 10-year deceased donor kidney transplant outcomes, 1997-2013

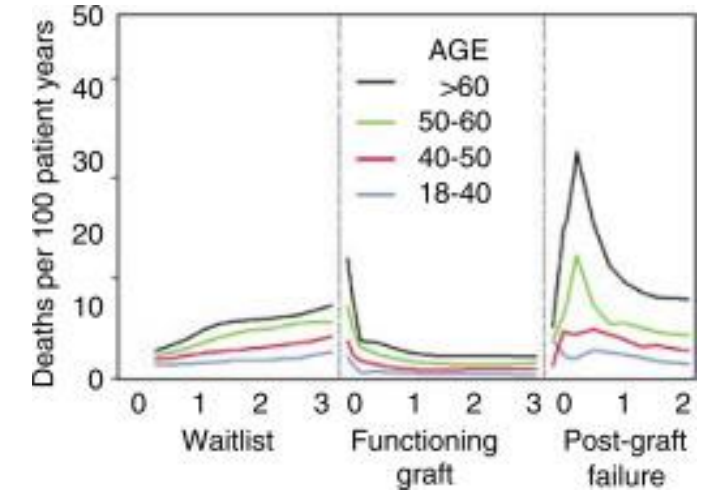
	One year post-transplant			Five years post-transplant			Ten years post-transplant		
Year	Prob. of all-cause graft failure	Prob. of return to dialysis or repeat transplant	Prob. of death	Prob. of all-cause graft failure	Prob. of return to dialysis or repeat transplant	Prob. of death	Prob. of all-cause graft failure	Prob. of return to dialysis or repeat transplant	Prob. of death
1997	13.9%	8.1%	6.1%	34.2%	23.4%	19.2%	57.9%	41.0%	39.3%
1998	13.5%	8.3%	5.5%	33.2%	23.5%	18.2%	56.4%	40.3%	38.0%
1999	14.3%	8.4%	5.9%	33.4%	22.7%	18.8%	56.3%	39.2%	38.2%
2000	13.7%	7.9%	6.4%	34.0%	22.7%	19.7%	56.7%	38.6%	39.2%
2001	12.7%	7.6%	5.7%	32.9%	21.1%	19.8%	55.2%	36.7%	38.6%
2002	12.7%	7.8%	5.6%	32.5%	21.8%	18.8%	53.5%	35.8%	37.1%
2003	12.4%	7.3%	5.6%	31.7%	20.3%	18.4%	54.4%	35.8%	37.6%
2004	11.8%	7.1%	5.4%	31.2%	20.5%	18.3%	53.1%	35.4%	36.7%
2005	11.5%	6.9%	6.0%	29.9%	19.1%	17.8%			
2006	10.8%	6.6%	5.1%	29.3%	18.7%	17.1%			
2007	9.8%	5.9%	4.6%	28.2%	17.7%	16.9%			
2008	9.6%	6.0%	4.5%	26.8%	16.1%	16.3%			
2009	9.4%	5.6%	4.9%	26.8%	16.3%	16.1%			
2010	8.8%	5.4%	4.4%						
2011	7.3%	4.3%	3.9%						
2012	7.8%	4.8%	3.8%						
2013	7.7%	4.8%	3.5%						

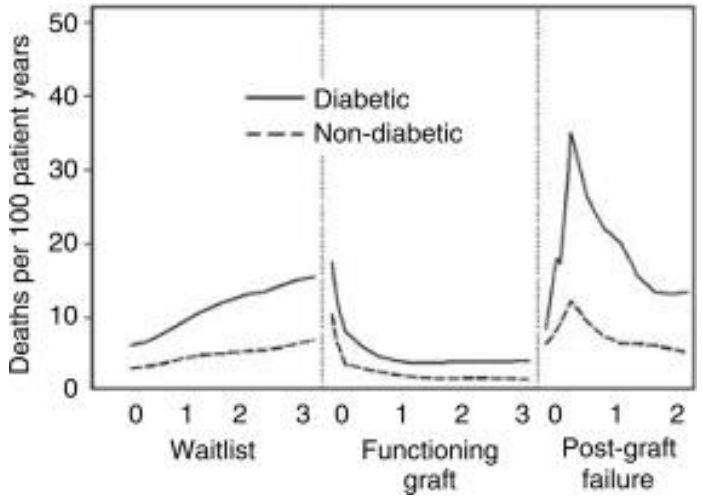
USRDS
United States Renal Data System

Transitions between Transplantation and Dialysis

	Years: 1995-2003		
	Wait-listing	Functioning graft	Dialysis return
▪ Patients (n)	89202	43433	5461
▪ Age (yrs,SD)	49.6(13.0)	49.2(13.2)	47.9(13.5)
▪ Male (%)	60.1	61.7	60.7
▪ Dialysis before waiting list (mths)			
< 12	56.5	63.3	65.9
12-23	26.7	24.3	23.5
≥ 24	16.8	12.4	10.6
▪ Deaths, n(%)	10836(12.2)	4927(10.4)	1474(27.0)
Sepsis, n(%)	1562(14.4)	539(10.9)	230(15.6)
CHF, n (%)	4891(45.1)	788(16.0)	553(37.5)

$$\text{Death per 100 patient years} = \frac{\text{Deaths (n)}}{\text{Sum of observation period of each patient}}$$

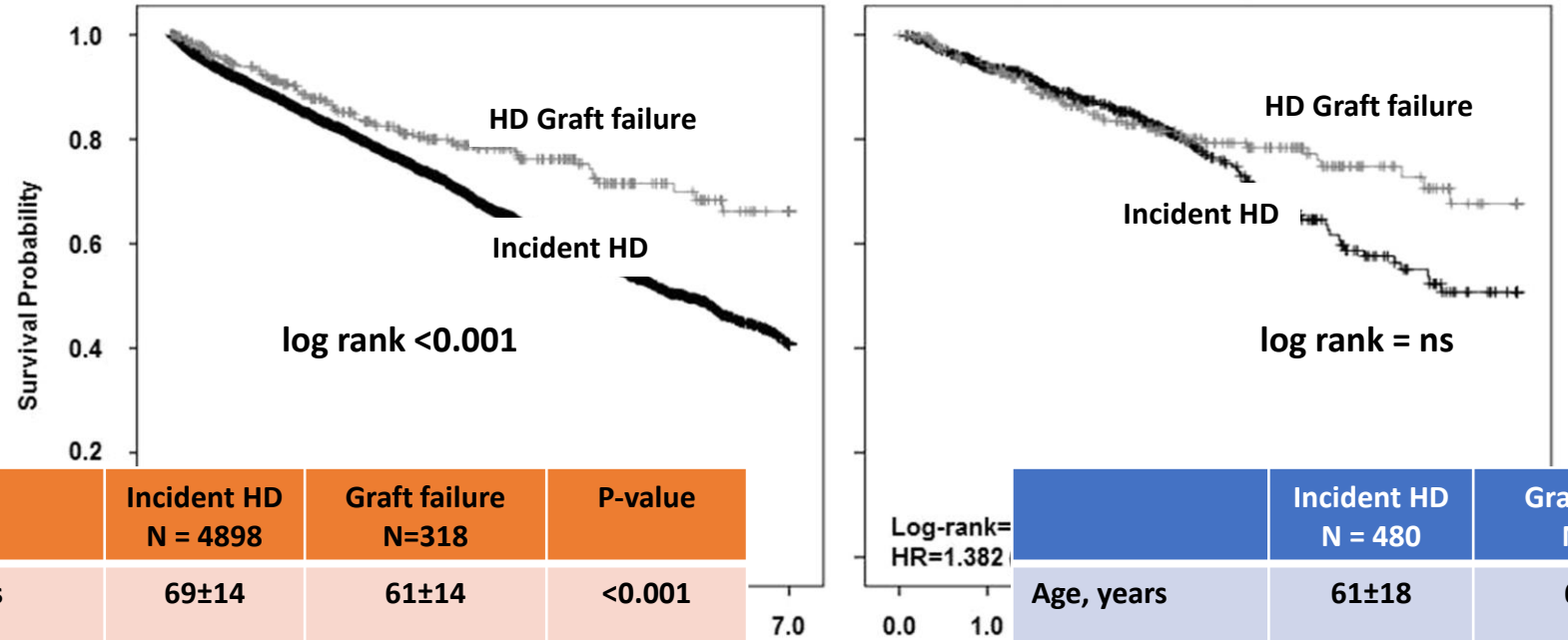




Gill JS, et al. Kidney Int. 2007;71(5):442-7.

Back to Dialysis after Graft Failure vs. Incident Dialysis Patients

Survival: Full cohort → **Propensity Score Adjusted**



	Incident HD N = 4898	Graft failure N=318	P-value
Age, years	69±14	61±14	<0.001
Charson score	3.1±1.3	2.8±1.1	<0.001
Female (%)	35	65	<0.001
Fistula (%)	46	66	<0.001
HDF (%)	62	44	<0.001
Qb, ml/min	380±56	400±55	<0.001
Hb, gr/dL	10.3±1.5	10.3±1.5	ns

	Incident HD N = 480	Graft failure N=240	P-value
Age, years	61±18	61±13	ns
Charson score	2.7±1.1	2.8±1.0	ns
Female (%)	64	63	ns
Fistula (%)	61	64	ns
HDF (%)	46	45	ns
Qb, ml/min	400±51	400±52	ns
Hb, gr/dL	10.2±1.6	10.3±1.5	ns

Varas J et al. Nephrol Dial Transplant, Volume 34, Issue 4, April 2019, Pages 667–672, https://doi.org/10.1093/ndt/gfy215

Original Report: Transplantation

American Journal of Nephrology

Am J Nephrol 2017;45:180–186
DOI: 10.1159/000455015

Received: November 9, 2016
Accepted: December 5, 2016
Published online: January 21, 2017

Mortality after Renal Allograft Failure and Return to Dialysis

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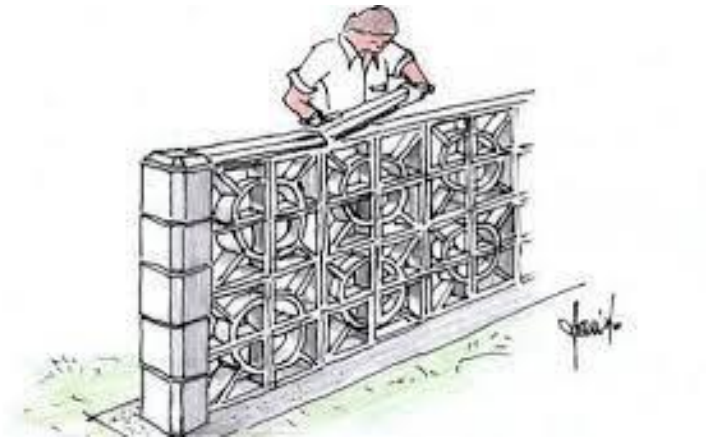
Edem Timpo[a] Rahul M. Jindal[d] Robert Nee[e,f] Nabil Sumrani[c]
Devon John[c] Fasika Tedla[a] Moro O. Salifu[a]

Variables	Adjusted Hazard Ratio	95% Confidence Interval	P-value
Age, years	1.033	1.027-1-038	<0.0001
AVF vs CVC	0.778	0.643-0.943	0.01
Graft vs CVC	0.58	0.398-0.847	0.005
Overweight vs normal BMI	0.854	0.749-0.973	0.02
Underweight vs normal BMI	1.305	1.076-1.583	0.006
Albumin < 3.5gr%	1.329	1.180-1.496	<0.0001
Peripheral arterial disease	1.404	1.211-1.628	<0.0001
Cerebrovascular disease	1.431	1.211-1.691	<0.0001

Managing Patients with Failing Kidney Allograft
Many Questions Remain

Scott Davis [1,2,3] and Sumit Mohan [1,2,3]

CJASN 17: 444–451, 2022. doi: https://doi.org/10.2215/CJN.14620920



Immunosoppressione

1. Transizione al Belatacept per ridurre la perdita di GFR
2. Ottimizzare il bilancio tra i rischi di infezione e di rigetto
3. Décalage in base alla possibilità di un secondo trapianto
4. Evitare la nefrectomia

Ritrapianto

1. Identificare un donatore vivente
2. Inserimento in lista «preemptive» appena GFR < 20 ml/minuto
3. Ottimizzare l'immunosoppressione se disponibile un donatore
   Ritrapianto tempestivo in base al GFR
4. Reclutamento del donatore vivente

Raccomandazioni per la Transizione

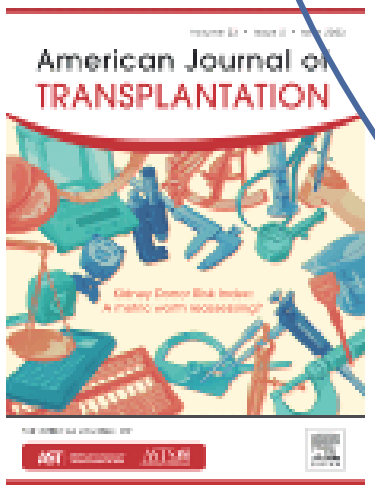
1. Gestione dell'anemia e dell'iperparatiroidismo
2. Accesso vascolare o catetere peritoneale tempestivo
3. Identificare la necessità di cure palliative
4. Identificare la necessità di early referral
5. Consigliare la tipologia di dialisi compresa la dialisi domiciliare

Received: 1 February 2021 | Revised: 23 April 2021 | Accepted: 20 May 2021
DOI: 10.1111/ajt.16737

COMPREHENSIVE REVIEW

AJT

The failing kidney allograft: A review and recommendations for the care and management of a complex group of patients



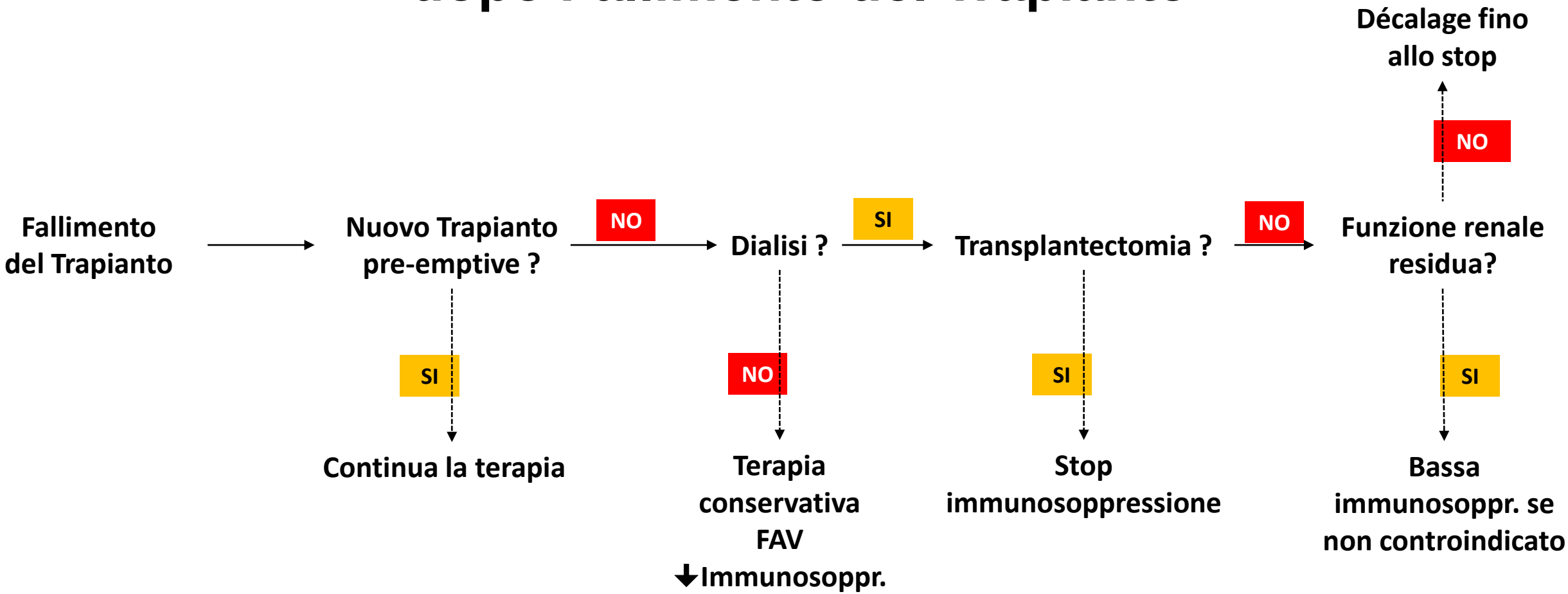
Repeat Transplant Candidate
- Avoid sensitization
- Facilitate pre-emptive transplant
- Avoid transplant nephrectomy

Residual Renal function
- Avoid rejection
- Avoid graft intolerance
- Improve transition to dialysis

Complications of Immunosuppression
- Infections
- Malignancy
- Atherosclerotic disease

Lubetzky M, et al s. Am J Transplant. 2021;21(9):2937-2949.

La Gestione della Terapia Immunosoppressiva dopo Fallimento del Trapianto

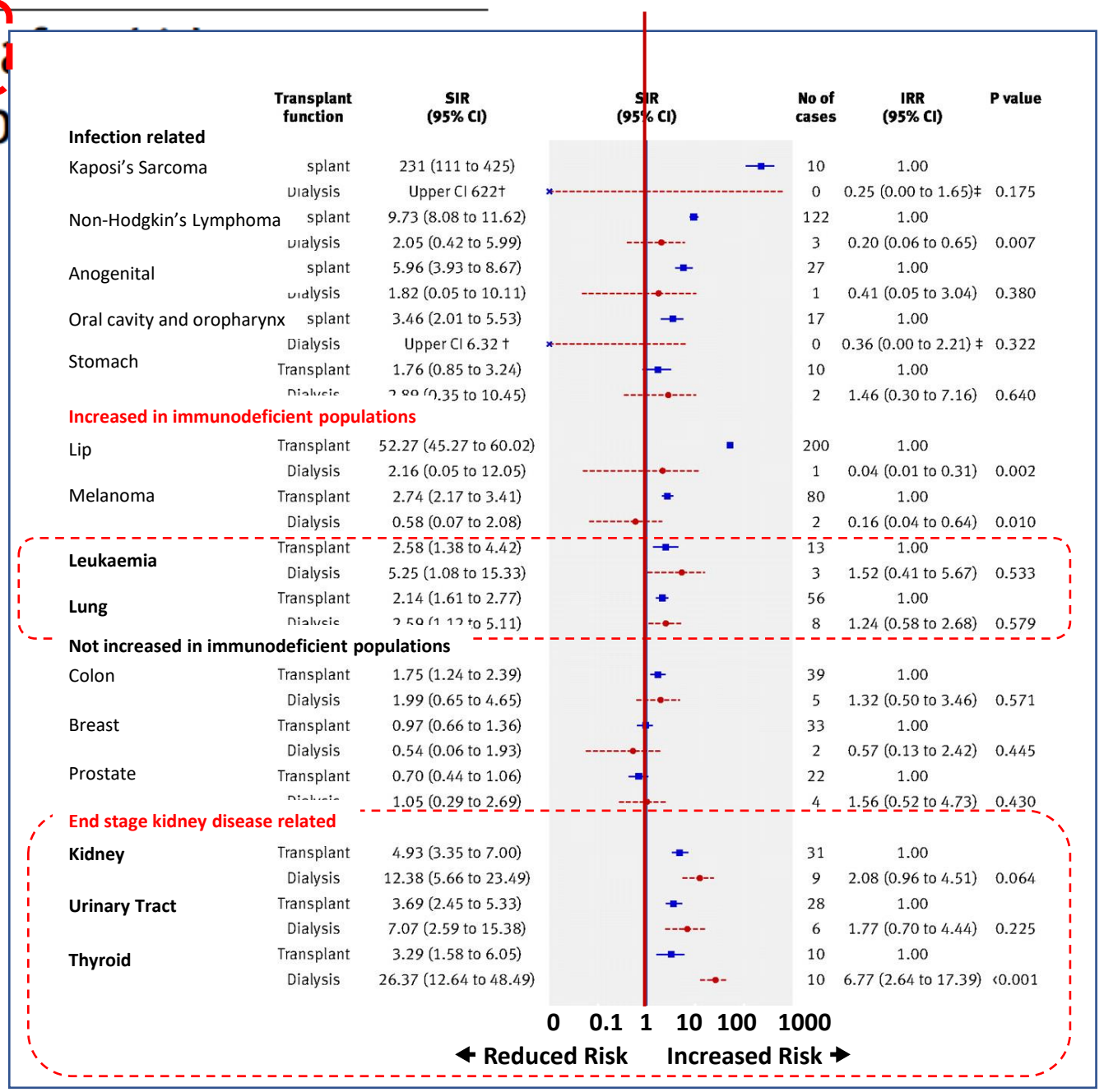


Fiorentino M, et al. Clin Kidney J. 2020 Jul 13;14(1):98-106.

Effect of reduced immunosuppression a transplant failure on risk of cancer: pop retrospective cohort study

- 1 January 1982 – 30 September 2003, patients(n) = 7,809
- Failure of the first renal transplant, (%) = 23
- Second renal transplant, (%) = 9
- Three or more renal transplant, (%) = 1

ANZ DATA | AUSTRALIA & NEW ZEALAND DIALYSIS & TRANSPLANT REGISTRY



van Leeuwen MT et al. British Medical Journal. 2010; 340: c570.

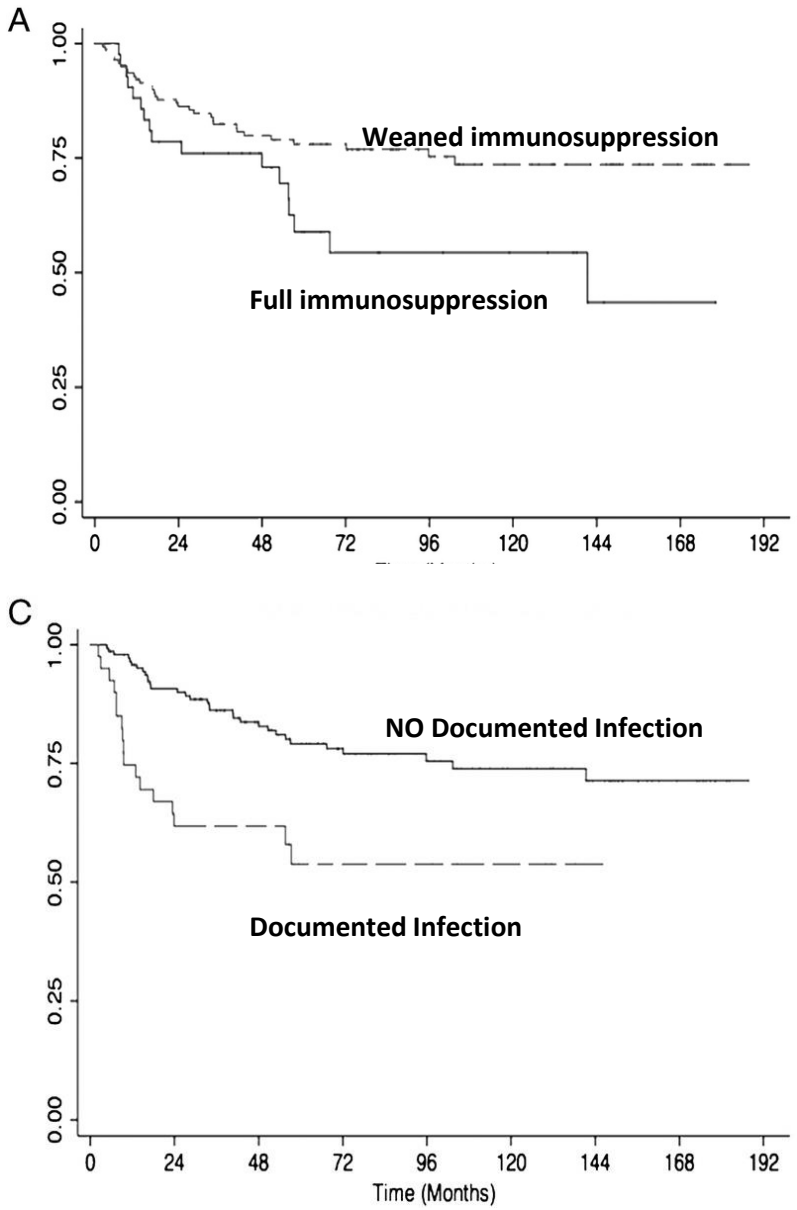
Fever, Infection, and Rejection After Kidney Transplant Failure

Kenneth J. Woodside,[1] Zachary W. Schirm,[1] Kelly A. Noon,[1] Anne M. Huml,[2] Aparna Padiyar,[2] ıund Q. Sanchez,[1] Nagaraju Sarabu,[2] Donald E. Hricik,[2] James A. Schulak,[1] and Joshua J. Augustine[2,3]

IMMUNOSUPPRESSION	WEANED n = 143	FULL N = 43	P-value
Age, years	46 ± 14	43 ± 11	Ns
Females, (%)	46	40	ns
Duration TX, months	72 (1-306)	92 (1-276)	ns
Living donor, (%)	27	14	ns
Hospitalization with fever (%)	45	40	ns
Hospitalization with infection (%)	17	35	0.01
Allograft nephrectomy (%)	42	26	0.05

Woodside KJ, et al. Transplantation. 2014 Mar 27;97(6):648-53.

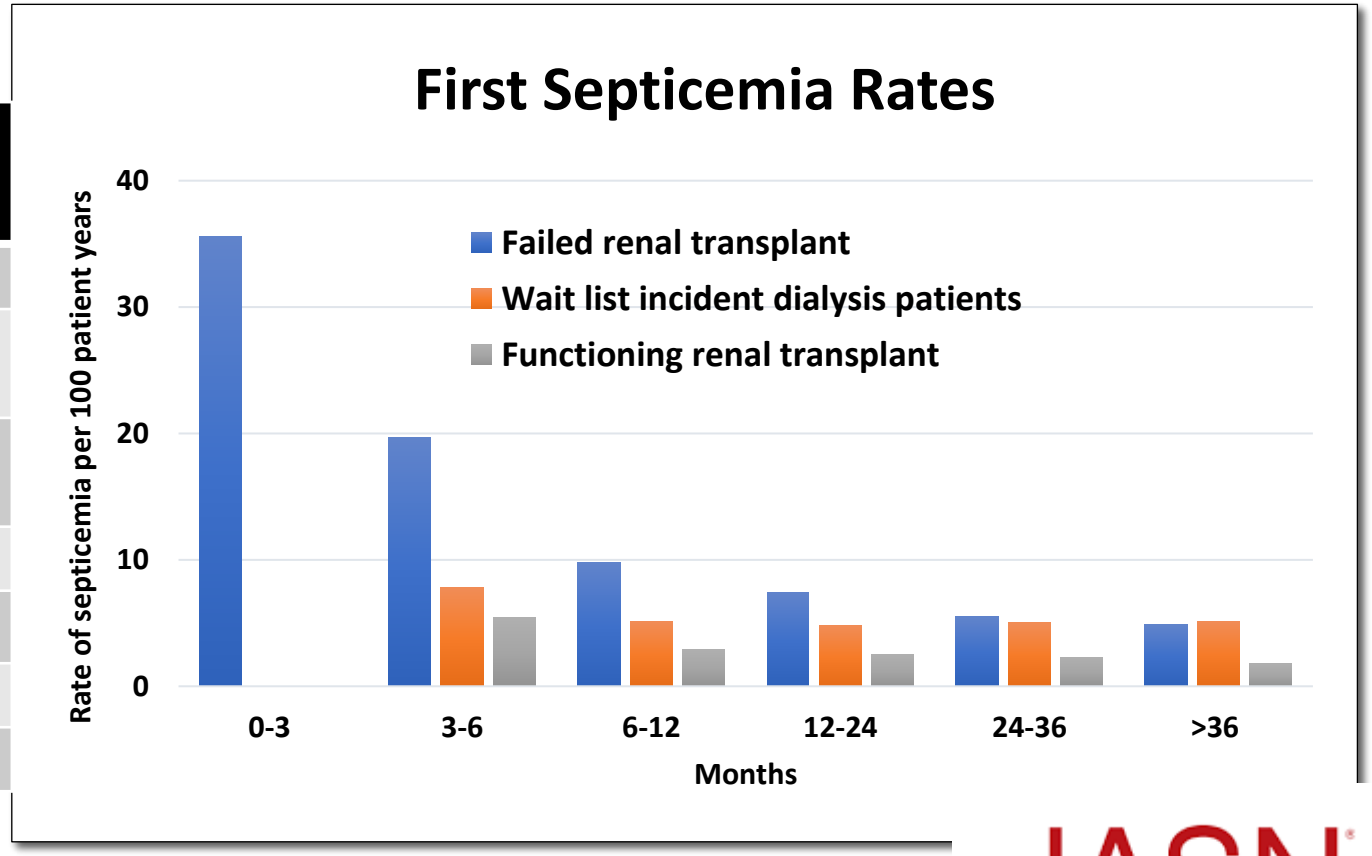
PATIENT SURVIVAL



Prevention of Sepsis during the Transition to Dialysis May Improve the Survival of Transplant Failure Patients

Olwyn Johnston, Nadia Zalunardo, Caren Rose, and John S. Gill
Division of Nephrology, University of British Columbia, St. Paul's Hospital; Vancouver, British Columbia, Canada

Variables	Hazard Ratio	95% CI	P-value
Septicaemia	2.93	2.64-3.24	<0.001
Multiple sepsis episodes	1.47	1.26-1.73	<0.001
Age at transplant failure ≥ 60	2.20	1.98-2.46	<0.001
BMI ≥ 30	0.84	0.74-0.96	0.01
Diabetes	1.89	1.70-2.09	<0.001
Cadaveric donor	1.23	1.10-1.39	<0.0001
Ischemic heart disease	1.57	1.33-1.85	<0.0001



JASN

Johnston O, et al. J Am Soc Nephrol. 2007;18(4):1331-7.

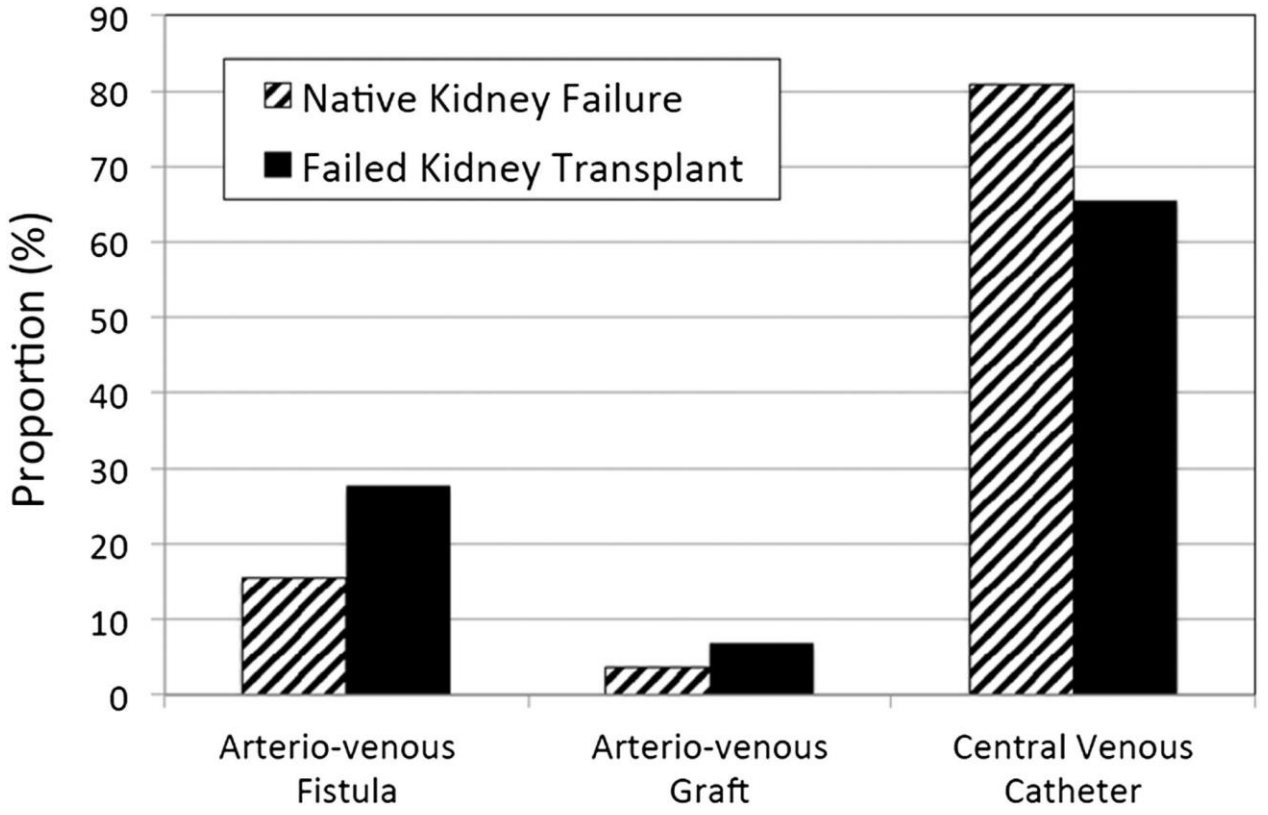
Initial Vascular Access Type in Patients with a Failed Renal Transplant

Micah R. Chan, Bharvi Oza-Gajera,* Kevin Chapla,* Arjang X. Djamali,*† Brenda L. Muth,* Jennifer Turk,* Maureen Wakeen,* Alexander S. Yevzlin,* and Brad C. Astor*‡*

- 1 January 2006 – 30 September 2011
- Patients (n) = 16,728 Kidney allograft failure
- Patients (n) = 509, 643 Native kidney failure

Dialysis Start

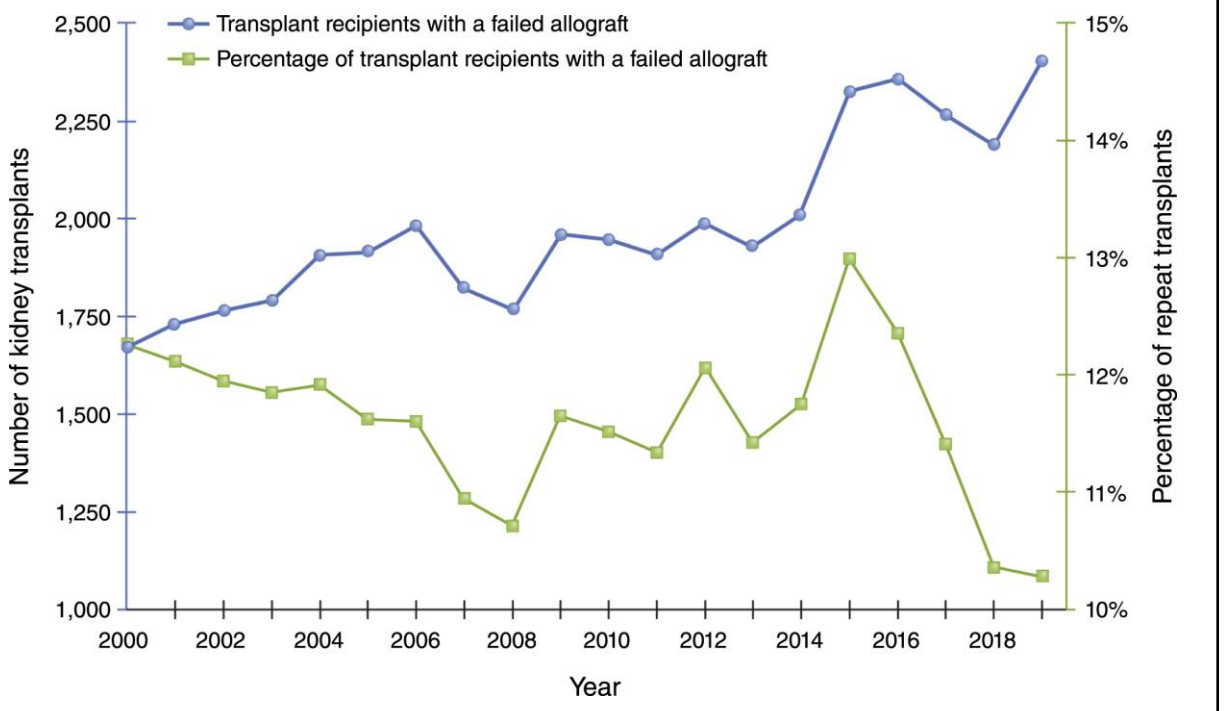
Variables	Hazard Ratio	95% CI	P-value
Age (per 10 yrs)	0.85	0.84-0.87	<0.001
Women	1.75	1.63-1.87	<0.001
Afro-American	0.77	0.72-0.83	<0.001
PVD	1.31	1.16-1.48	<0.001
Diabetes	1.14	1.06-1.22	0.001
Institutionalized	1.53	1.23-1.89	<0.0001
None Nephrology Referral	2.00	1.72-2.33	<0.0001



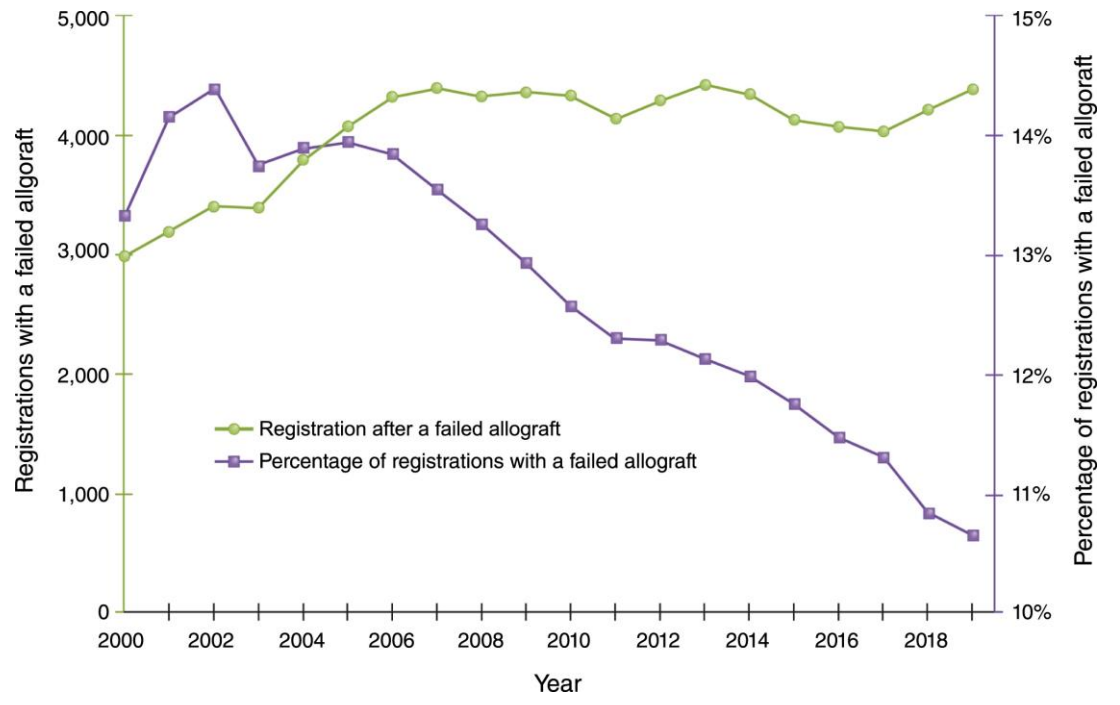
Chan MR, et al. Clin J Am Soc Nephrol. 2014;9(7):1225-31.

Kidney Transplant after a Failed Allograft

Trapianti eseguiti



Inserimenti in Lista d'Attesa



Davis S, Mohan S. Clin J Am Soc Nephrol. 2022 Mar;17(3):444-451.

Indicazioni alla Transplantectomia dopo Trapianto di Rene

Prima di 12 mesi dal Trapianto

1. Perdita precoce del trapianto
2. Trombosi vascolare
3. Rigetto acuto
4. Rigetto iperacuto
5. Infezione urinaria ricorrente o sepsi

Dopo 12 mesi dal Trapianto

1. Infiammazione cronica
2. Nefropatia da Polyomavirus
3. Cancro
4. Sindrome da intolleranza del Graft
5. Infezione urinaria ricorrente o sepsi

Fiorentino M, et al. Clin Kidney J. 2020 Jul 13;14(1):98-106.

Sindrome da Intolleranza del Graft

Sintomi e segni <u>comuni</u>

- **Febbre**
- **Macroematuria**
- **Edema perirenale**
- **Nefromegalia**
- **Tensione del Graft**

Sintomi e Segni <u>meno comuni</u>

- **Malessere generale**
- **Calo ponderale**
- **Trombocitopenia**
- **Resistenza all'EPO**
- **Aumento PCR e VES**

Lubetzky M, et al s. Am J Transplant. 2021;21(9):2937-2949.

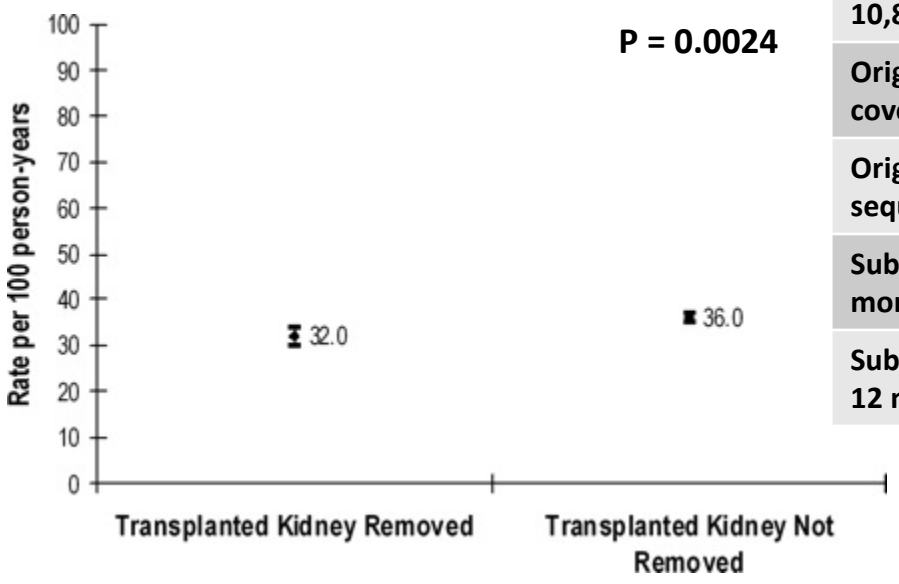
CLINICAL RESEARCH www.jasn.org

Transplant Nephrectomy Improves Survival following a Failed Renal Allograft

Juan Carlos Ayus,* Steven G. Achinger,† Shuko Lee,‡ Mohame
Alan S. Go[¶]

USRDS
United States Renal Data System

- 1 January 1994 – 31 December 2004
- Total USRDS patients (n) = 10,951
- Allograft nephrectomy,(n) = 3,451 (31.5%)



Analysis	Adjusted Hazard Ratio for Death for Nephrectomy vs. NON Nephrectomy	95% Confidence Interval
Original cohort (n = 10,951)	0.69	0.63-0.74
Original cohort with adjustment for transplant center (n = 10,951)	0.69	0.63-0.74
Original cohort + patients whose transplants failed < 90 days after initial transplant date (n = 13,702)	0.67	0.63-0.71
Subset of original cohort who survived ≥ 30 days after transplant failure (n = 10,886)	0.69	0.66-0.74
Original cohort + patients without documented Medicare fee-for-service coverage within 90 days after transplant failure (n = 14,352)	0.67	0.63-0.72
Original cohort + patients with two transplant in which the transplant sequence was uncertain or unknown (n = 11,237)	0.68	0.63-0.73
Subset of original cohort whose duration of transplant before failure was < 12 months (n=1545)	0.76	0.65-0.90
Subset of original cohort whose duration of transplant before=failure was ≥ 12 months (n=9,318)	0.65	0.60-0.71

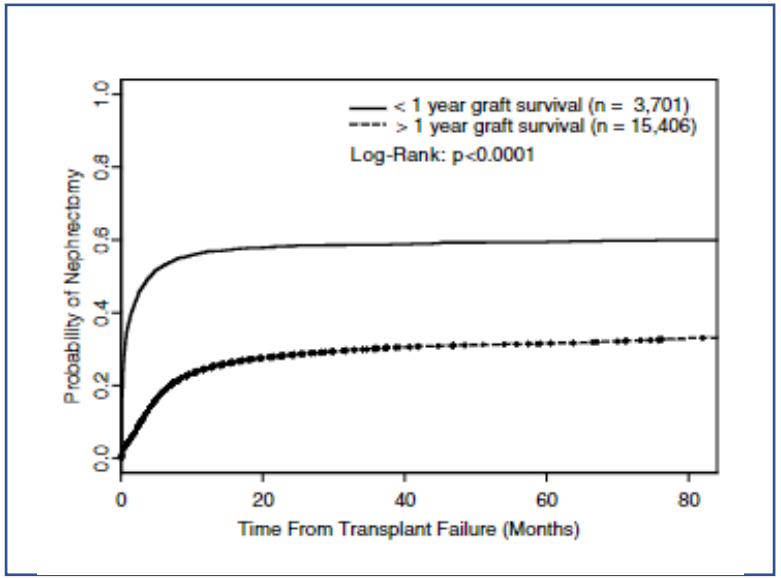
Ayus JC, et al. J Am Soc Nephrol. 2010;21(2):374-80.

American Journal of Transplantation 2007; 7: 1961–1967
Blackwell Munksgaard

doi: 10.1111/j.1600-6

Nephrectomy After Transplant Failure: Current Practice and Outcomes

O. Johnston[a], C. Rose[a], D. Landsberg[a], W. A. Gourlay[b] and J. S. Gill[a,c,*]



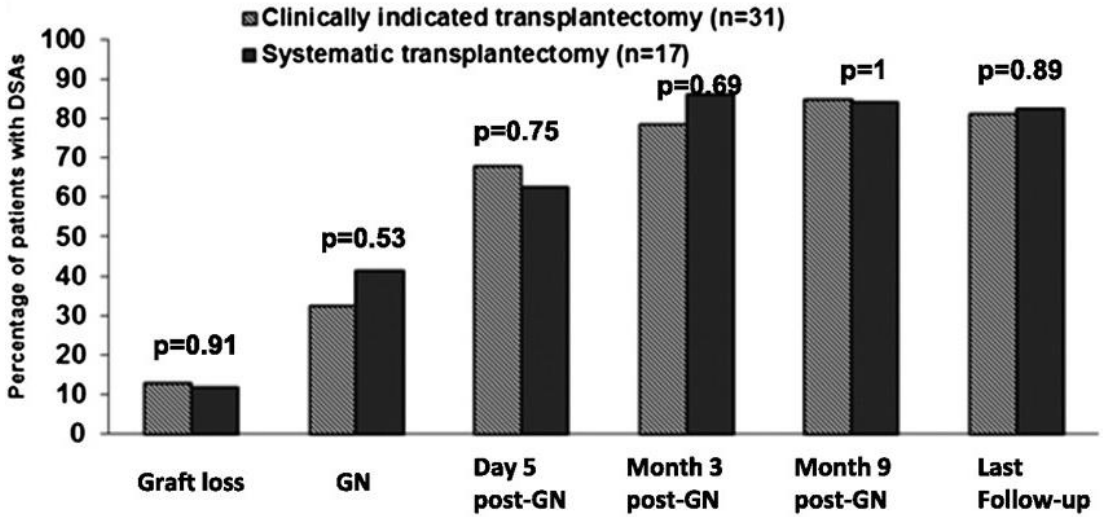
SHORT TERM COMPLICATIONS	Graft survival < 1 year N = 2,094	Graft survival < 1 year N = 4,119	P-value
• Events during hospital admission			
Myocardial infarct	0.9%	0.5%	NS
Congestive heart failure	4.0%	2.7%	<0.01
Sepsis	6.1%	2.9%	<0.0001
Death	1.0%	1.1%	NS
• Events within 90 days of hospital admission			
Myocardial infarct	1.5%	1.1%	NS
Congestive heart failure	7.1%	7.5%	NS
Sepsis	10.7%	6.2%	<0.0001
Death	5.0%	4.7%	NS

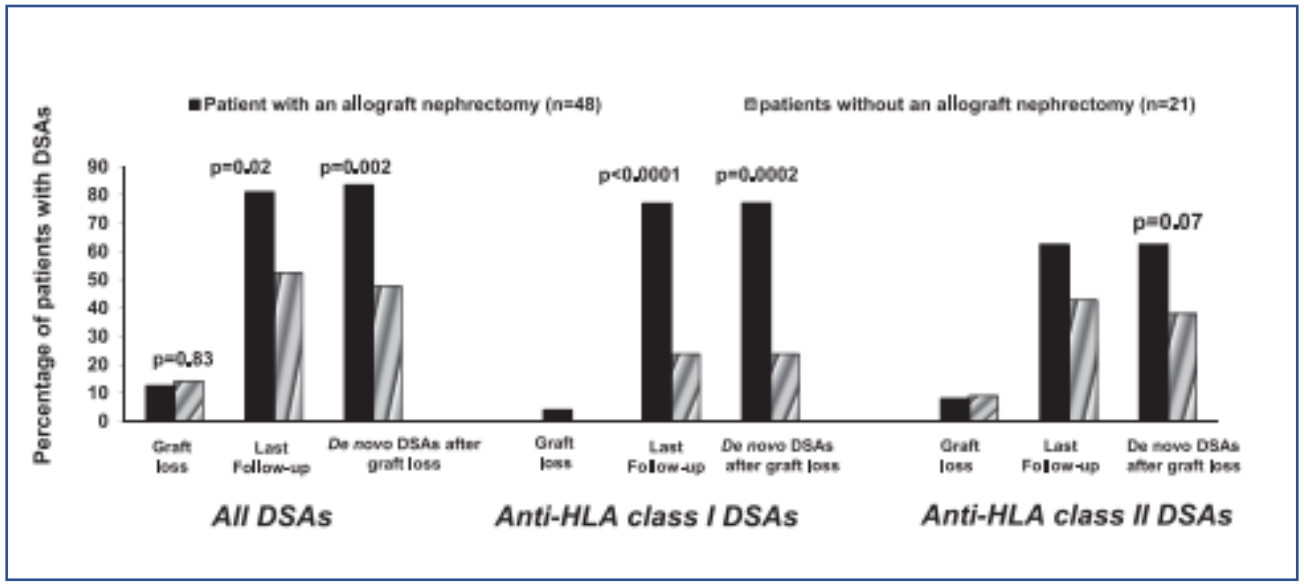
	Patients with EARLY graft failure		Patients with LATE graft failure	
	DEATH	SEPSIS	DEATH	SEPSIS
Hazard ratio	1.13	1.09	0.89	0.88
95% CI	1.01-1.26	0.95-1.24	0.83-0.95	0.81-0.96

Donor-Specific Antibodies after Ceasing Immunosuppressive Therapy, with or without an Allograft Nephrectomy

Arnaud Del Bello, Nicolas Congy-Jolivet,†‡ Federico Sallusto,§ Celine Guilbeau-Frugier,‖ Isabelle Cardeau-Desangles,* Marylise Fort,‡ Laure Esposito,* Joelle Guitard,* Olivier Cointault,* Laurence Lavayssière,* Marie Béatrice Nogier,* Antoine Blancher,†‡ Lionel Rostaing,*¶ and Nassim Kamar*¶*

*D

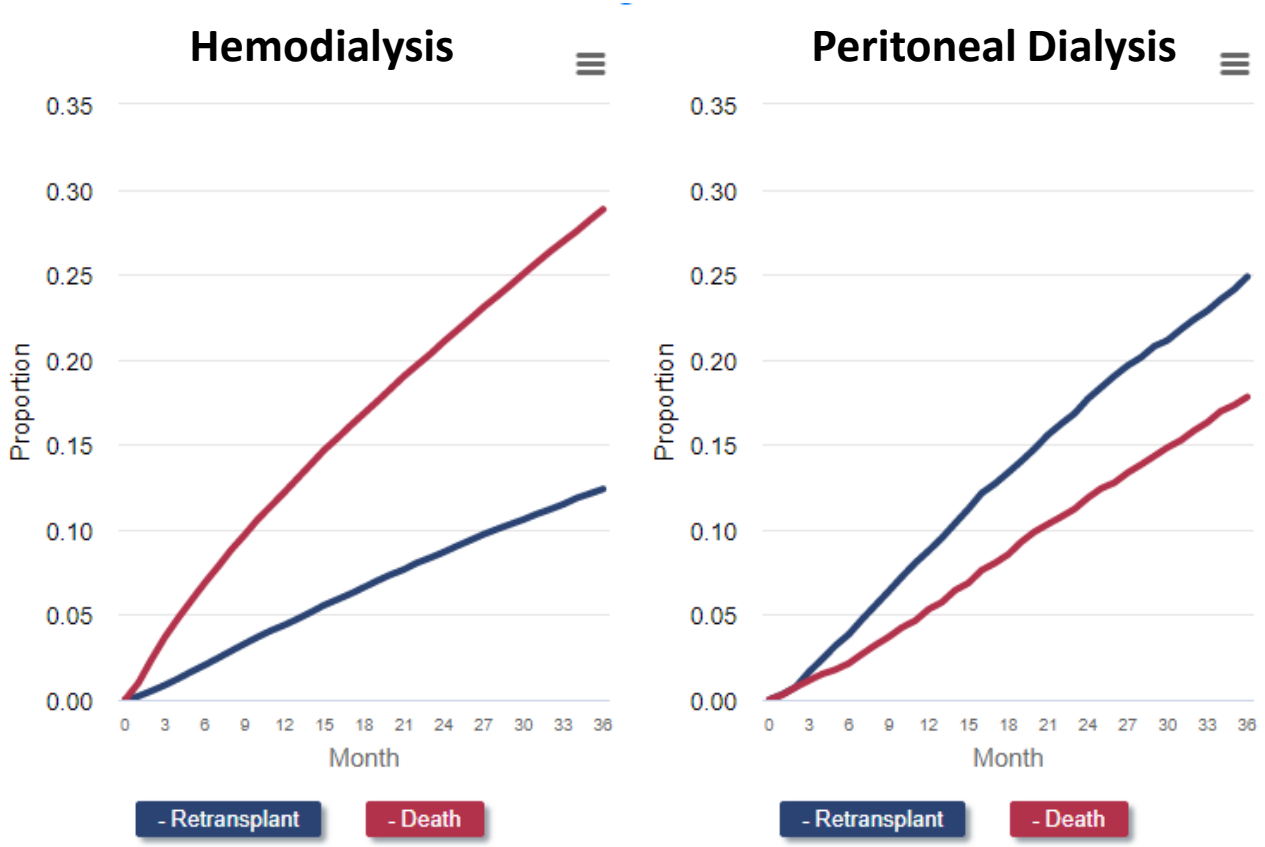




- ❖ **February 2007 – July 2008, patients (n) = 31**
  Clinically indicated
- ❖ **July 2008- November 2010 , patients (n) = 17**
  Systematic transplantectomy

Del Bello A, et al. Clin J Am Soc Nephrol. 2012;7(8):1310-9.

Death or Retransplant after a Failed Allograft



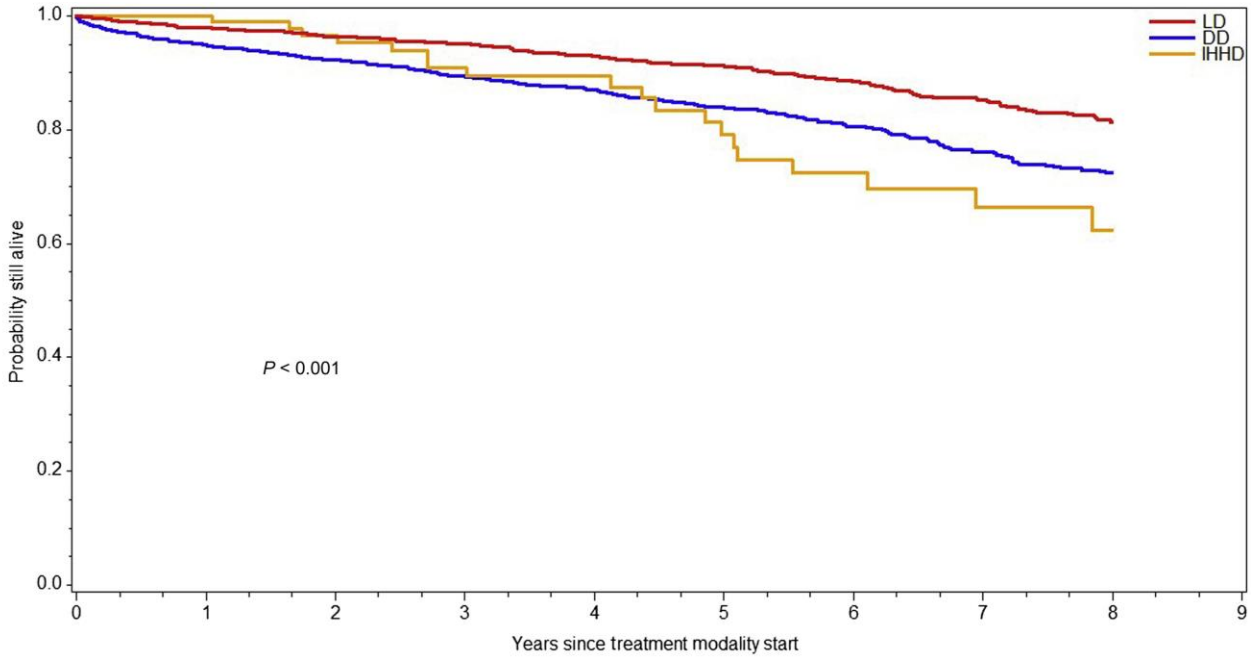
KI REPORTS
KIReports.org
CLINICAL RESEARCH

Intensive Home Hemodialysis Survival Comparable to Deceased Donor Kidney Transplantation

Angie G. Nishio-Lucar[1,3], Subhasish Bose[1,2,3], Genevieve Lyons[1], Kwabena T. [illegible]
Jennie Z. Ma[1] and Robert S. Lockridge Jr[1,2]

Intensive Home Hemodialysis
Hemodialysis treatment 4 or more times per week, preferably totalling 20 hours or more and eliminating the 2 day interdialytic gap.

- **IHHD = 116 patients**
- **Living donor KT = 1212 patients**
- **Deceased donor KT = 1834 patients**

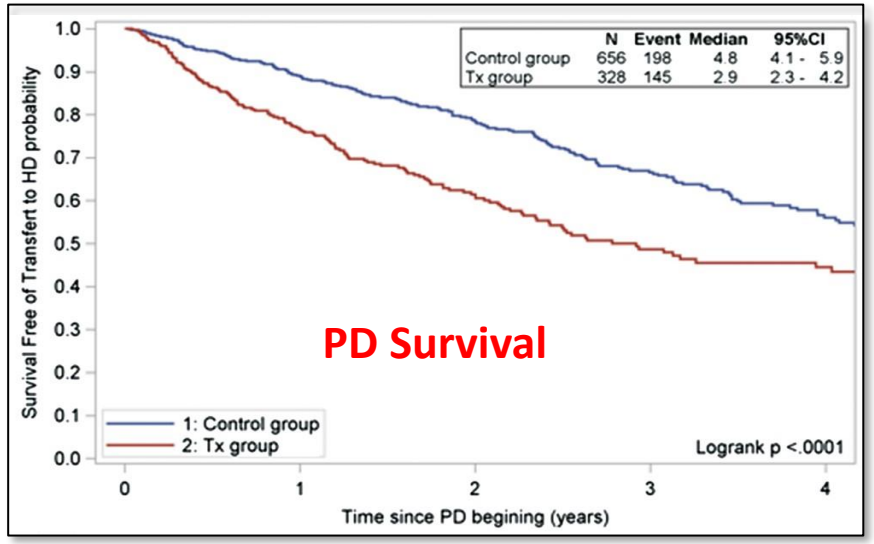


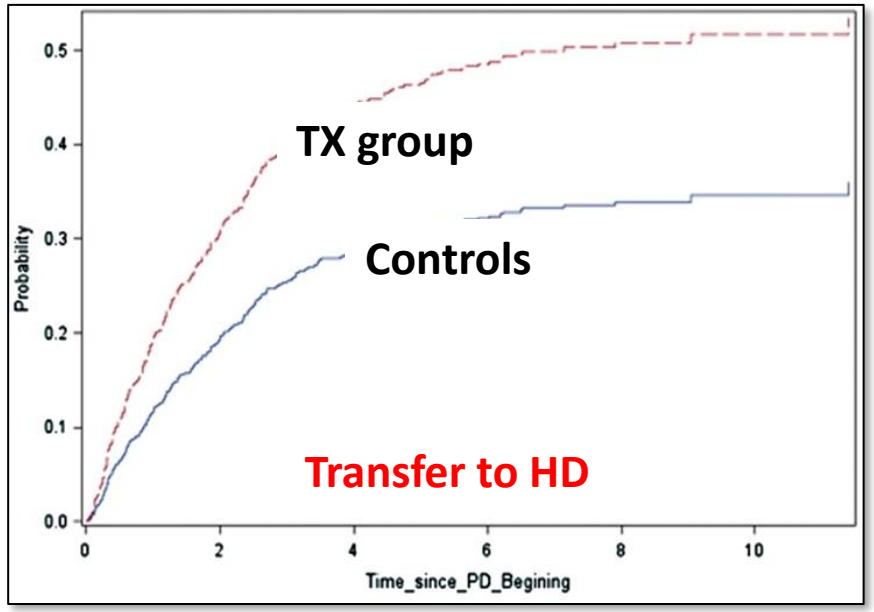
	DD KT vs IHHD		LD KT vs IHHD	
Modal Type	**Hazard ratio (95%CI)**	**P -value**	**Hazard ratio (95%CI)**	**P -value**
Unadjusted	**0.92 (0.80-1.41)**	**ns**	**0.53 (0.34-0.83)**	**0.005**
Adjusted	**0.96 (0.62-1.48)**	**ns**	**0.69 (0.44-1.08)**	**ns**
PS-adjusted	**0.96 (0.62-1.49)**	**ns**	**0.60 (0.37-0.96)**	**ns**
PS-adjusted	**1.06 (0.46-2.49)**	**ns**	**0.80 (0.47-1.35)**	**ns**

Outcome della Dialisi Peritoneale dopo il Fallimento del Trapianto

	PD post Tx group N= 328	Control PD group N= 656
Age, years	50(19.5-82.6)	50.8(18.2-91.4)
Male, n (%)	166(50.6)	341(52)
Charlson score	4 (3-11)	4 (3-14)
Diabetes, n(%)	45 (13.7)	162 (24.7)

Fattori Predittivi	Odds Ratio	95% CI	P-Value
Età, per anno	0.99	0.98-0.99	0.03
Uomini	0.75	0.60-0.93	0.01
Fallimento TX	1.62	1.30-2.01	<0.0001
Peritoniti	1.38	1.12-1.71	0.002

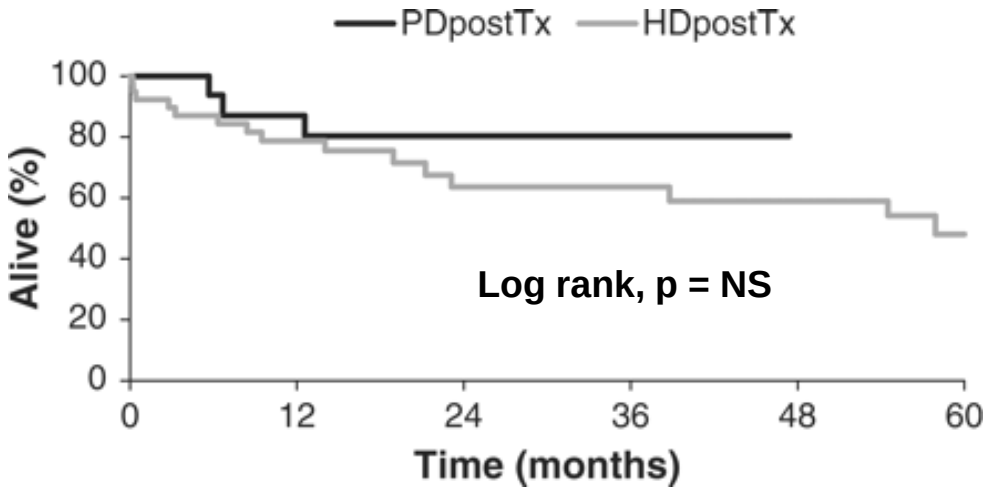


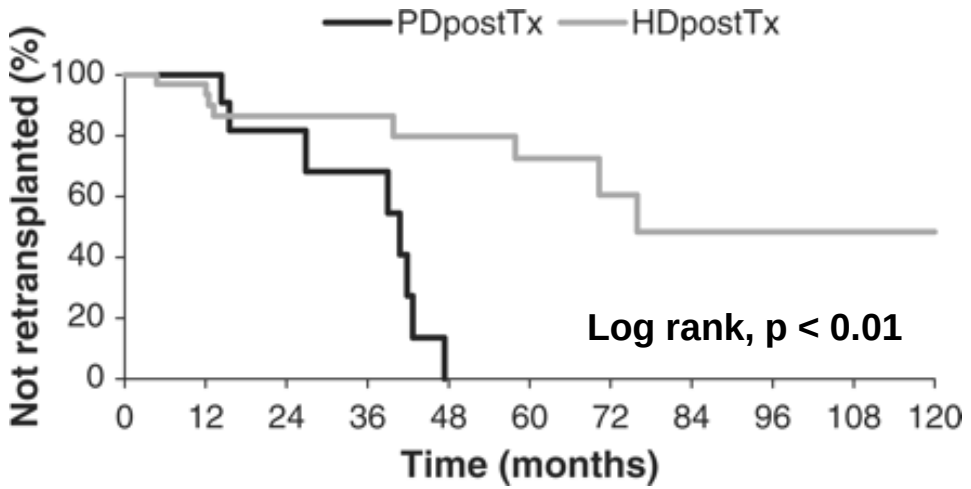


Benomar M, et al from the French Language Peritoneal Dialysis Registry (RDPLF). Nephrol Dial Transplant. 2019;34(5):858-863.

Dialisi Peritoneale vs Emodialisi dopo Fallimento del Trapianto

	PD post TX N= 21	HD post TX N= 39
Age, years	46 (36-57)	49(34-60)
Males, (%)	43	62
Duration TX, months	144 (27-176)	59 (9-131)
CRP, mg/L	14 (10-39))	20 (6-38)





de Jonge H, et al. Nephrol Dial Transplant. 2006;21(6):1669-74.

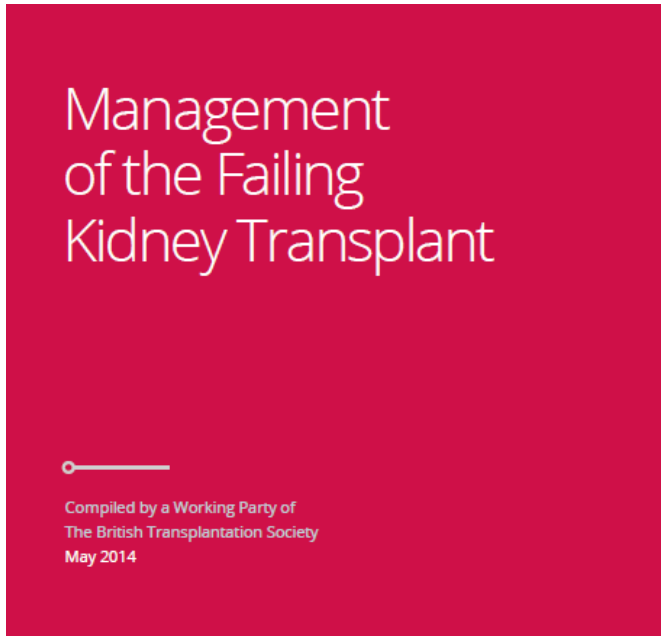
Reduced survival and quality of life following return to dialysis after transplant failure: the Dialysis Outcomes and Practice Patterns Study

DOPPS
Dialysis Outcomes and Practice Patterns Study

- DOPPS 1-2-3 (1996-2008)
- Patients (n) = 1,856 Kidney allograft failure
- Patients (n) = 2, 806 Native kidney failure
- SF-36: eight scales, score 0-100
- KDQOL-SF: three scales, score 0-100
- PCS: Physical component summary
- MCS: Mental component summary

		TN patients N = 2806	TF patients N= 1856	P-value	TF patients			P-value
					< 3 months (n=313)	3-12 months (n=299)	12 months (n=1244)	
PCS	Physical component summary	39.6	37.1	<0.0001	36.4	36.5	37.4	Ns
SF-36	Physical functioning	54.2	47.3	<0.0001	46.2	47.7	47.4	Ns
SF-36	Role Physical	42.3	34.7	0.0007	25.9	30.8	37.5	0.03
SF-36	General health	46.9	42.4	0.0005	41.0	40.4	43.1	Ns
SF-36	Bodily pain	66.3	60.8	0.0001	59.1	59.4	61.4	Ns
MCS	Mental component summary	46.5	44.8	Ns	43.5	43.9	45.3	Ns
SF-36	Mental health	65.1	61.5	Ns	59.2	61.5	62	Ns
SF-36	Role emotional	59.6	55.8	Ns	49.5	54.2	57.6	Ns
SF-36	Social functioning	65.8	60.6	0.02	60.6	56.1	61.6	Ns
SF-36	Vitality	45.5	38.8	0.0002	33.7	38.5	40.0	Ns
KDQOL-SF	Burden	40.4	38.2	Ns	40.4	35.9	38.3	0.002
KDQOL-SF	Effects	61.5	57.3	Ns	60.0	55.8	57.1	0.0004
KDQOL-SF	Symptoms	75.3	72.3	0.02	71.0	70.8	72.9	Ns

Nephrol Dial Transplant. 2012 Dec;27(12):4464-72



Psychosocial Issues

1. **Graft failure can have profound psychological effects on patients (depression, suicidal ideation) and close family members**
2. **There is often psychological resistance from both the patient and clinician to accept that a transplant is failing**
3. **When transplant failure occur patients are often ill-prepared to cope with the emotions experienced**
4. **Common emotions are grief, guilt, anger, loss of self esteem, and fear**
5. **Transplanted patients may be out of touch with current treatments and need to receive up to date information**

Take Home Messages